

**AMENDMENT UNDER 37 C.F.R §1.111**

U.S. Serial No.: 09/585,475

IN THE CLAIMS:

Please cancel claims 7, 8 and 9 without prejudice or disclaimer. Further, kindly amend the claims as follows:

1. (Amended) A method for determining a degree of toxicity or efficacy of an agent candidate not previously known to have toxicity or efficacy comprising:  
exposing a tissue of interest in a subject to the agent such that the agent contacts said tissue of interest.

a<sup>1</sup>  
obtaining a test biological sample containing protein from said tissue of interest.

measuring levels of protein markers of toxicity or efficacy in said sample, and  
comparing the levels of said markers to the levels of the same markers in a control sample or other sample exposed to known toxic or known effective agents to determine whether the tissue of interest in a subject is experiencing toxicity or an effective response or the degree of such responses.

4. (Amended) The method of claim 1 further comprising:

measuring levels of individual proteins in a proteome of said biological sample from the tissue of interest.

a<sup>2</sup>  
comparing these levels with levels of the same proteins in the proteome from a sample from a tissue of interest from a control subject or a subject treated with one or more other agents known to be toxic or effective, and

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detecting which protein levels are increased or decreased by a statistically significant amount.

5. (Amended) The method of claim 1 wherein the statistically significant amount is determined at  $p < 0.01$ .

10. (Amended) The method of claim 1 wherein the levels of protein markers in the test biological sample are compared to the levels of the same protein markers in biological samples exposed to a known effective agent or known toxic agent.

11. (Amended) The method of claim 4 wherein the levels of protein markers in the test biological sample are compared to the levels of the same protein markers in biological samples exposed to a known effective agent or known toxic agent.

12. (Amended) The method of claim 4 wherein said individual proteins in said proteome are separated by two-dimensional electrophoresis.

13. (Amended) The method of claim 1 wherein the comparing is to the control and the control is a biological sample containing protein from the same tissue of interest before the tissue of interest is exposed to the agent.

Please add the following new claims:

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--85. A method for determining a degree of toxicity or efficacy of an agent comprising:

exposing a tissue of interest in a subject to the agent such that the agent contacts said tissue of interest,

obtaining a test biological sample containing protein from said tissue of interest,

measuring levels of at least one protein marker selected from the group consisting of the markers of Table 8 except for MSN 34, MSN 79, MSN 182, MSN 204, MSN 347, MSN 413, MSN 633, MSN 933, MSN 1001 and MSN 1250 and comparing the levels of said markers to the levels of the same markers in a control sample or other sample exposed to known toxic or known effective agents to determine whether the tissue of interest in a subject is experiencing toxicity or an effective response or the degree of such toxicity or response.

86. The method of claim 85 wherein said protein marker is selected from the group of markers of Table 9 except for MSN 204, MSN 347, MSN 633 and MSN 1001.

87. The method of claim 85 wherein plural protein markers are measured.

88. The method of claim 87 wherein the levels of protein markers determines the relative amount of toxicity or effectiveness.

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89. The method of claim 87 wherein the levels of protein markers in the test biological sample are compared to the levels of the same protein markers in biological samples exposed to known effective agent or known toxic agent.
90. The method of claim 89 wherein the agent is a pharmaceutical suspected of having the same mechanism of action as said known effective agent and it is given in a pharmaceutically appropriate amount.
91. The method of claim 90 wherein the agent is an antilipemic agent.
92. The method of claim 85 wherein the comparing is to the control and the control is a biological sample containing protein from the same tissue of interest before the tissue of interest is exposed to the agent.
93. The method of claim 10 wherein the agent is a pharmaceutical suspected of having the same mechanism of action as said known effective agent and is given in a pharmaceutically appropriate amount.
94. The method of claim 93 wherein the agent is an antilipemic agent.
95. A method for determining a degree of toxicity or efficacy of an agent candidate not previously known to have toxicity or efficacy comprising;